REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated October 14, 2009 are respectfully requested. Claims 1-11 and 20-23 are pending.

I. Amendments

Claim 1 is amended to recite that the delivery system is comprised of a gemini surfactant and a nucleic acid. Basis is found, for example, on page 8, line 20 ("*Biologically active agents which can be used with the present invention include, but are not limited to, nucleic acids....*"). Claim 1 is also amended to recite that the gemini surfactant is one having a spacer with a length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16. Basis is found, for example, in Table 1 on page 27 and on page 8, lines 1-14.

Dependent claim 4 is amended for consistency with the changes to claim 1.

II. Rejections Under 35 U.S.C. § 102

Claims 1-4 and 6-10 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Camilleri et al. (PCT Publication No. WO99/29712; "Camilleri").

Claims 1-4 and 6-10 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by Wheeler (US Patent No. 6,696,424; "Wheeler").

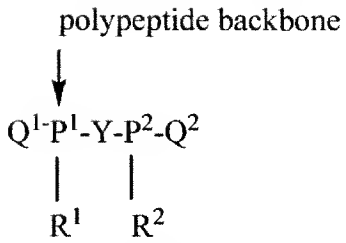
These rejections are respectfully traversed.

A. The Present Claims

The present claims are directed to a topical delivery system comprising a gemini surfactant in admixture with a nucleic acid, where the gemini surfactant is one having a spacer with length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16. The delivery system, when in contact with skin or a mucosal membrane, provides a therapeutic effect.

B. The Applied Art

CAMILLERI describes particular peptide-based gemini compounds as well as methods for their preparation. The compounds of Camilleri possess the following general structure:



where Q^1 and Q^2 are positively charged hydrophilic head groups formed from one or more amino acids and/or amines; P^1 and P^2 each make up a central portion having a polypeptide backbone and linked together by bridge, Y, and R^1 and R^2 are each a hydrophilic tail (Camilleri, page 2, lines 15-26). Camilleri further describes uses for such peptide-based compounds including antisense, gene therapy, and cell culture experiments (Camilleri, page 5, lines 9-24). Nowhere does Camilleri teach topical delivery, nor that a topical delivery system could provide a therapeutic effect.

WHEELER describes specific cationic lipid compounds for use as cytofectins and as adjuvants (Wheeler, col 6, lines 37-44). The cationic lipid compounds of Wheeler correspond to general formulas (I) or (II) therein (Col 6, lines 45-66 and Col 9, lines 19-47). Described are methods of use which include facilitating transfection and providing an enhanced humoral immune response (Col 3, lines 39-60), e.g., for vaccinations. Administration to skin (Col 16, lines 44-46) and across a mucous membrane (Col 16, lines 61) is contemplated.

C1. Legal Standard

The standard for lack of novelty, that is, for anticipation, is one of strict identity. To anticipate a claim for a patent, a single prior source must contain all its essential elements. M.P.E.P. § 2131.

M.P.E.P. § 2173.05(g) states:

> A functional limitation must be evaluated and considered...for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. A functional limitation is often used in association with an element, ingredient, or step of a process to define a particular capability or purpose that is served by the recited element, ingredient, or step.

C2. Analysis: Rejection Over Camilleri

The delivery system as claimed includes the following elements: (i) a gemini surfactant having a spacer with length corresponding to $(CH_2)_n$, where $n = 3, 4, 6$, or 16; and (ii) that the delivery system, when in contact with skin or a mucosal membrane, provides a therapeutic effect.

In contrast, and with respect to element (i), the gemini compounds disclosed by Camilleri are shown on page 2 of Camilleri and reproduced above. As seen, the spacer or "central portion" of the Camilleri gemini surfactants is of the general structure "P^1-Y-P^2", where P^1 and P^2 are polypeptides and Y is a bridge or linker group, such as a disulphide bond or $(CH_2)_m$, where m is 1-6 (page 3, lines 19-20). Because the gemini surfactants described by Camilleri are not the same as the gemini surfactant in the claimed topical delivery system, Camilleri does not anticipate.

With respect to element (ii), Applicants first note the legal standard set forth in M.P.E.P. § 2173.05(g) that requires functional limitations to be considered, particularly in the context of being associated with an ingredient to define a particular capability of the recited ingredient. In the present claims, and as expressly set forth in the data in Table 1 on page 27 of the application as filed, gemini surfactants with a spacer having a length corresponding to $(CH_2)_n$, where $n = 3, 4, 6$, or 16 are effective to deliver sufficient nucleic acid through the skin or mucosal membrane to provide a therapeutic effect. Gemini surfactants of different spacer lengths do not necessarily provide this effect, as illustrated in the data of Table 1.

Camilleri is silent with respect to topical or transdermal delivery of a nucleic acid. Camilleri does not teach that topical delivery of a nucleic acid with mixed with a gemini surfactant with a spacer having a length corresponding to $(CH_2)_n$, where $n = 3, 4, 6$, or 16 could provide a therapeutic effect, as claimed. Since this effect is not contemplated by Camilleri, the compositions described by Camilleri do not anticipate. Moreover, since the gemini surfactants described by Camilleri are different from the gemini surfactants of the claimed topical delivery system, the compositions of Camilleri (1) are not inherently useful for topical delivery or (2) do not inherently provide for or achieve the claimed therapeutic effect.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102.

C3. Analysis: Rejection Over Wheeler

The delivery system as claimed includes the following elements: (i) a gemini surfactant having a spacer with a length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16; and (ii) that the delivery system, when in contact with skin or a mucosal membrane, provides a therapeutic effect.

With respect to element (i), the gemini compounds disclosed in Wheeler are of the general form set forth in Formula I and Formula II on Col. 6 and Col 8, respectively. The spacer (R^9 in Formula I and R^{11} in Formula II) is a linker that can be any one of the thousands of compounds listed on Col. 7, line 15 to Col. 8, line 54. Specifically, Wheeler teaches that the linker can be a:

> carbohydrate, a polysaccharide, an amino acid, a peptide, a polypeptide, a protein, an antibody, a peptidomimetic, a polyamine or a histone (Col. 7, lines 12-17); or that the linker can be the polyamines spermine and spermidine (as well as derivatives thereof), and proteins rich in basic amino acids such as arginine and histidine (or derivatives or analogues thereof). Cationic substances such as the histones, spermines and spermidines are known to bind and modulate negatively-charged cell membrane surfaces. For example, lipid-derivatized spermine-like structures efficiently modulate gene transfer into mammalian endocrine cells (Behr, J-P. et al., Proc Natl Acad Sci USA 86:6982-6986 (1989)). Other preferred proteins useful as linkers include immunoglobulins (e.g., single chain immunoglobulins, immunoglobulin fragments), transferrin, asialoglycoproteins (e.g., asialofetuin), integrins, cytokines (e.g., interferons and interleukins), selectins, cell surface receptors, receptor ligands, major histocompatability proteins, lysosomotrophic proteins, extracellular proteins, proteins bearing internalization and/or nuclear localization signals, excreted proteins, protein hormones (e.g., insulin, erythropoetin), growth factors (e.g., human growth factor, insulin-like growth factor, epidermal growth factor), bacterial exotoxins, low density lipoprotein, alpha-2-macroglobulin, and angiotensin. In addition, fusion proteins and chimeric proteins comprising advantageous DNA binding and/or targeting properties alone or in combination are also contemplated as preferred linkers. In certain preferred embodiments, where the cationic lipid compound is according to formula (I), the linker is optionally substituted C1 to C10 alkyl or alkyloxy, or optionally substituted C1 to C10 alkenyl or alkenyloxy. In certain other embodiments, the linker preferably comprises a ureyl linkage (i.e., --

NR--C(O)--NR--, where R is H or optionally substituted C1 to C10 alkyl or alkenyl), a bis-ureyl linkage (i.e., --NR--C(O)--NR--R'--NR--C(O)--NR--, where R is H or optionally substituted C1 to C10 alkyl or alkenyl, and R' is optionally substituted C1 to C10 alkyl or alkenyl), or a peptide linkage (i.e., --C(O)--NR--, where R is H or optionally substituted C.sub.1 to C.sub.10 alkyl or alkenyl).

The legal standard for determining whether a claims to a species is anticipated by a laundry listing, or genus, in a prior art reference is set forth in M.P.E.P. 2131.02. According to the M.P.E.P., a broad genus does not anticipate a claimed species where one skilled in the art would have to choose judiciously from the dozens of possibilities to arrive at the claimed species. That is, a prior art laundry listing will only anticipate a claim to a species if a person of ordinary skill is able to "at once envisage" the specific claimed compound from the prior art genus. For example, in In re Ruschig (45 U.S.P.Q. 274 (C.C.P.A. 1965)), the court held that a genus of 130 or 156 compounds with widely different substituents did not anticipate a claimed species.

From the listing above, it is clear that Wheeler describes thousands of possible gemini surfactants. There is no guidance in Wheeler's listing from which a skilled artisan would arrive at gemini surfactants having a spacer with a length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16.

Moreover, and with respect to the presently claimed element that the delivery system provide a therapeutic effect when applied to the skin or mucosal membrane, there is no showing in Wheeler of which, if any, gemini surfactants would provide for topical delivery of a nucleic acid in sufficient amounts for a therapeutic effect. A skilled artisan, based on the teaching in Wheeler, is in no way guided or led to the presently claimed gemini surfactants.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102.

III. Rejections Under 35 U.S.C. § 103

Claims 1, 4 and 5 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Wheeler U.S. Patent No. 6,696,424 in view of Weiner et al., U.S. Patent No. 5,981,505 ("Weiner"). This rejection is respectfully traversed for the following reasons.

A. The Present Claims

The claimed subject matter is summarized above.

B. The Applied Art

WHEELER is summarized above.

WEINER describes methods for introducing nucleic acids into cells for expression of a desired protein. The nucleic acid is packaged in a genetic construct along with certain regulatory elements, such as a promoter and a polyadenylation signal, to express the protein.

C1. Analysis: Legal Standard

An obviousness analysis is informed by consideration of the factors stated in *Graham v. John Deere*, 383, U.S. 1, 148 USPQ 459 (1966). That is, the factors which must be considered in an inquiry directed to the obviousness or non-obviousness of an invention are as follows:

(i) scope and content of the asserted art

(ii) differences between claimed subject matter and the asserted art; and

(iii) the level of ordinary skill in the art.

In this analysis, the cited references must be viewed without the benefit of hindsight afforded by the claimed subject matter or accompanying specification.

C2. The scope and content of the combined teachings of Wheeler in view of Weiner differs from the claimed subject matter.

The claimed topical delivery system comprises a gemini surfactant having a spacer with a length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16. The delivery system, when in contact with skin or a mucosal membrane, provides a therapeutic effect.

As discussed above, Wheeler does not show or suggest a topical delivery system comprised of a gemini surfactant as claimed. Weiner is cited merely for its teaching of a genetic construct, and does not mention gemini surfactants. Accordingly, the combined teachings of Wheeler and Weiner fail to show or suggest each and every claimed element, and therefore a prima facie case of obviousness is not established.

Even if, *in arguendo*, the combined teachings of Wheeler and Weiner disclosed all of the claimed elements, the claimed delivery system produces an unexpected result in view of

the cited art. As noted in the recent Supreme Court decision *KSR International Co. v. Teleflex Inc.*, S. Ct. 1727 (2007); 82 USPQ2d 1385, 1397 (2007), one early and still recognized test for nonobviousness of a claimed combination is whether the combination produces more than could be predicted from the prior art.

As shown in Table 1, on page 27 of the application as filed, delivery systems with a gemini surfactant as claimed, i.e., one having a spacer with a length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16, provide significantly higher levels of transfection than delivery systems comprised of a gemini surfactant with other spacer lengths. Specifically, gemini surfactants with spacer lengths corresponding to $(CH_2)_n$, where n is 3, 4, 6, and 16 achieved high transfection levels compared to gemini surfactants with spacer lengths corresponding to $(CH_2)_n$, where n is 6, 8, or 10. This result could not be known or predicted based on the combined teachings of the cited art.

Because a skilled artisan would not have had a reasonable expectation of success in achieving the a therapeutic response upon topical application of the claimed delivery system, the claimed system is not obvious in view of the cited art. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

IV. Double-Patenting Rejection

Claims 1-4 and 6-10 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-38 of application serial no. 12/215,963. This rejection is respectfully traversed in view of the claim amendments and following remarks.

In determining whether a nonstautory basis exists for a double patenting rejection, the first question to be asked is - does any claim in the application define merely an invention that is merely an obvious variation of an invention claimed in the patent?. M.P.E.P. 804 II.B.1.

The present claims are directed to a topical delivery system comprising a gemini surfactant having a spacer with length corresponding to $(CH_2)_n$, where n = 3, 4, 6, or 16. Claim 1 of the 12/215,963 application is directed to a topical delivery system comprising a gemini surfactant having a spacer comprised of a hydrophilic substituent, such as an aza, imino, hydroxyl or ether moiety. Because of this difference in the spacers of the gemini surfactant as claimed in the instant delivery system and as set forth in the claims of the pending 12/215,963 application, the present claims are not an obvious variation of the

claims in the 12/215,963 application. Accordingly, withdrawal of the obviousness-type double patenting rejection is respectfully requested.

Alternatively, and in the event the Examiner does not withdraw the obviousness-type double patenting rejection, Applicants respectfully request the rejection be held in abeyance until allowable subject matter is identified.

V. Conclusion

In view of the foregoing, the claims pending in the application patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 590-0734.

No fees are believed due with this communication. However, the Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-4616.

Respectfully submitted,
King & Spalding LLP

Date: January 14, 2010

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